REMARKS

Claims 1-66 are pending in the application, claims 4, 6-37, 44-57, 65 and 66 are withdrawn from consideration, claims 1,3, and 58 have been amended, and new claims 67-71 have been added. Support for the claim amendments and additions may be found throughout the specification, including the claims as originally filed. No new matter has been added.

Amendment of claims should in no way be construed as an acquiescence to any of the Examiner's rejections. The amendments to the claims are being made solely to expedite prosecution of the present application and do not, and are not intended to, narrow the claims in any way. Applicants reserve the option to further prosecute the same or similar claims in the instant or in a subsequent patent application.

Rejection of claims 1-3, 5, 38, 40-43, 58, 59 and 61-64 under 35 U.S.C 112, first paragraph

The Examiner rejected claims 1-3, 5, 38, 40-43, 58, 59, and 61-64 under 35 U.S.C. 112, first paragraph, "because the specification, while being enabling for the decision-tree analysis for the data-mining technique, does not reasonably provide enablement for any data mining technique."

As the Examiner knows, and in accordance with MPEP 2164.02, the test of enablement is whether one skilled in the art could make and use the claimed invention from the disclosure coupled with information known in the art without undue experimentation. United Stated v. Telectronics, Inc., 857 F.2d 778, 8 USPQ2d 1217 (Fed. Cir. 1988); In re Stephens, 188 USPQ 659 (CCPA 1976). The specification only needs to describe the invention in sufficient detail to enable a person skilled in the most relevant art to make and use the invention. (See MPEP 2164.05(b)). When an invention, in its different aspects, involves distinct arts, the specification is adequate if it enables the adepts of each art, those who have the best chance of being enabled, to carry out the aspect related to their specialty. In re Naquin, 158 USPQ 317 (CCPA 1968); Ex parte Zechnall, 194 USPQ 461 (Bd. of App. 1973); Ex Parte Billottet, 192 USPQ 413 (Bd. of App. 1976).

Applicants consider that one of ordinary skill in the data mining arts recognizes that there are multiple types and forms of data mining, with the illustrated (Figure 1) decision tree

technique in the present disclosure known to those of ordinary skill as a data mining method of comparatively simple computational complexity, and further, a method that can be easily illustrated. Such exemplary embodiment of Figure 1 in the present application, however, is not necessary to enabling even a decision tree embodiment, as decision trees are well-known in the art, and similarly, definitions or explanations of other exemplary embodiments for other data mining techniques are likewise unnecessary to enable one of ordinary skill to apply the various data mining techniques as claimed. Further, and with respect to the amended claims, it is clear as to the purpose of the data mining technique (i.e., to facilitate correlations and determinations of properties) such that one of ordinary skill in the data mining and database arts would readily understand how to practice the invention as claimed.

In support of Applicants' position, Applicants attach herein portions of a presentation, the entirety of which can be found at http://www-users.cs.umn.edu/~mjoshi/hpdmtut/sld001.htm, where the first attached slide demonstrates data mining tasks as including classification, clustering, association rule discovery, etc. Subsequent slides (some attached herein) refer in further detail to data mining techniques that optionally use, for example, decision trees, memory-based (case-based) reasoning, neural networks, and Bayesian techniques, among others. These and other data mining techniques are well-documented in the prior art as having applications in the data mining arts, with the various options often compared with respect to computational complexity and data correlation/independence, among other factors. The Applicants' demonstration of one data mining technique, as provided by Figure 1, is necessarily sufficient to disclose to one of ordinary skill how to employ not only one, but all of such alternative, well-documented data mining techniques. Applicants note that decision trees, Bayesian classifiers, and other such data mining concepts have been in the art for decades.

To further demonstrate the level of ordinary skill in the data mining arts, Applicants invite the Examiner to perform an electronic/internet search using the various data mining terms, and Applicants contend that such search will provide Examiner with many search results indicating the close integration of varying data mining techniques. Applicants provide here two further examples that provide comparisons of some data mining techniques: http://citeseer.nj.nec.com/MachineLearning/PatternRecognition/hubs.html; and, http://ai.rightnow.com/colloquium/papers/machine_learning_in_IR.pdf.

Applicants thus remind Examiner of MPEP 2164.04, which states that "[a]ll assertions made that the enabling disclosure is not commensurate in scope with the protection sought by the claims must be supported by (1) evidence or (2) reasoning substantiating doubts so expressed." In re Dinh-Nguyen, 181 USPQ 46 (CCPA 1974). Mere conclusionary statements as to the level of ordinary skill in the art are not a sufficient basis for a 112 first paragraph rejection. In re Brebner, 173 USPQ 169 (CCPA 1972). Notwithstanding the aforementioned regarding enablement rejections, Examiner fails to provide any evidence or reasoning substantiating Examiner's basis for the 112 first paragraph rejection. Accordingly, Applicants consider that Examiner fails to shift the burden of enablement to the Applicants. Nonetheless, Applicants remarks herein provide multiple examples indicating the state of the prior art and the uncontroverted enablement of Applicants' claims based on the state of the prior art of data mining at the time of application filing.

Applicants thus traverse Examiner's rejection of claims 1-3, 5, 38, 40-43, 58, 59, and 61-64 under 35 U.S.C. 112, first paragraph, and based on the remarks and prior art herein, consider such claims to be enabled as required under 35 U.S.C. 112.

Rejection of claims 58-64 under 35 U.S.C. 112, first paragraph

Claims 58-64 were rejected under 35 U.S.C. §112, first paragraph, for reasons of enablement. The Action states that:

> "The instant application fails to provide guidance to one of ordinary skill in the art for modifying experimental procedures or modifying protein sequence for optimizing high-throughput protein expression as seen in claim 58. The specification does not provide or suggest what are the modifications of experimental procedures or protein sequences specific for high-throughput optimization thus not enabling one of ordinary skill in the art to know how [to] optimize the method described." (Office Action at 4)

The rejection is respectfully traversed.

Contrary to the assertions in the Office Action, the specification provides many examples of specific modifications to the experimental procedures that permit optimization of high throughput protein expression. For example, the specification teaches that the database may include various biochemical and/or biophysical properties that relate to expression such as data on expressability, or level of expression, of proteins produced in various vectors and hosts with various fusion tags and under various conditions, such as temperature and medium composition,

the protein yield obtained from various vectors and hosts under various conditions, etc. (see e.g., specification at page 7, lines 21-28). Furthermore, the specification teaches that the database may include information about growth conditions that optimize protein expression yield including, for example, length of incubation, temperature, time, induction conditions, etc. (see e.g., specification at page 8, lines 7-10). Further variables related to protein expression that may be included in the database include different types of expression vectors which may contain, for example, promoters, transcription/translation terminators, and/or ribosome binding sites, etc. (see e.g., specification at page 11, line 28 to page 12, line 2). Further, the specification discloses that data related to protein expression in a variety of hosts may be included, such as, for example, bacterial expression systems and eukaryotic expression systems for mammalian cells, yeast, and insect cells (see e.g., specification at page 12, lines 1-9).

Additionally, the specification provides sufficient teachings about modifications of protein sequences for optimization of high-throughput protein expression to enable one of ordinary skill in the art to make and use the claimed invention. For example, the specification teaches that database may include protein sequence information, such as, for example, primary amino acid sequence, amino acid composition, character of a region of a sequence, hydrophobicity, charge, molecular weight, presence and length of low complexity regions, percent of one or more specific amino acids in a sequence, percent of a combination of two or more amino acids, percent of amino acids of a general class, presence of charged regions, etc. (see e.g., specification at page 6, lines 10-23).

Claim 58 provides a method of optimizing high throughput protein expression using a database comprising protein sequence information, protein biochemical properties, and/or protein biophysical properties, such as, for example, the information as described above. The database may then be analyzed using a data-mining technique to correlate one or more of protein sequence, biochemical properties, and/or biophysical properties. For example, the database may be mined to correlate protein sequence with expressibility under the various conditions as described above. As taught in the specification such correlations between the protein sequence and biochemical and/or biochemical properties, such as protein expression, is useful in optimizing high-throughput strategies (see e.g., specification at page 14, lines 7-10). Additionally, the specification teaches that the diverse collection of proteins in the database is valuable for analysis aimed at identifying sequence features that are predictive of protein biophysical and/or biochemical behavior, such as protein expression (see e.g., specification at page 14, lines 28-29). Therefore, based on the teachings in the specification, one of ordinary skill in the art would be able to modify experimental procedures and/or protein sequence to optimize high-throughput protein expression based on the analysis of the database. For example, such analysis, and the correlations obtained thereby, may help to determine optimal conditions

for expression of one or more new protein based on the information contained in the database. Such information would help to optimize high-throughput protein expression because it would reduce the time necessary to optimize protein expression conditions. Alternatively, analysis of the database, and the correlations obtained thereby, may help to determine one set, or a few sets, of conditions that produce optimal protein expression for a diverse population of proteins. Such information would help to optimize high-throughput protein expression of a diverse population of proteins because it would eliminate the necessity for determining optimal conditions for each individual protein. Additionally, analysis of the database, and the correlations, obtained thereby, may help to identify elements of a protein sequence, such as, for example, character of a region of a sequence, hydrophobicity, charge, etc. that affect protein expression. Based on the teachings in the specification, one of skill in the art would be able to modify a protein sequence on the basis of the databases correlations to optimize protein expression.

Accordingly, the subject matter of claims 58-64 was clearly described in the specification in such a way as to enable one skilled in the art to make and/or use the invention. Therefore, reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. 112, first paragraph, is respectfully requested.

Rejection of claims 1-3, 5, 38-43, and 58-64 under 35 U.S.C. 112, second paragraph

Examiner rejected claims 1-3, 5, 38-43, and 58-64 under 35 U.S.C. §112, second paragraph, as being indefinite.

Specifically, Examiner rejects claim 1, stating it "is unclear what the action of correlation is between." Applicants amend independent claims 1 and 58 to more clearly state the claimed invention; however, Applicants consider that the previously filed independent claims clearly indicated that the correlations related to biochemical and biophysical properties of the protein sequences in the claimed database.

Examiner states that claims 1 and 58 are indefinite due to the "lack of clarity in the term 'protein sequence information.'" Applicants direct the Examiner to MPEP 2173.05(a) which states that the "meaning of every term used in a claim should be apparent from the prior art _or from the specification_ and the drawings at the time the application is filed." (emphasis added by Applicants) When the specification states the meaning that a term in the claim is intended to have, the claim is examined using that meaning, to achieve a complete exploration of the Applicant's invention and its relation to the prior art. In re Zletz, 893 F.2d 319, 13 USPQ2d

1320 (Fed. Cir. 1989) Applicants also direct the Examiner to the present specification, page 6, second paragraph (lines 10-23), which provides a meaning for the term "protein sequence information." Based on the above remarks, such independent claims 1 and 58 are thus not indefinite, as indicated by Examiner.

Examiner also states, with respect to independent claims 1 and 58, that "it is unclear if the database comprises protein sequence information of the protein of interest stated in the preamble, or if the information concerns other protein sequences that are known." Applicants direct the Examiner to basic claim construction rules regarding antecedent basis, and to MPEP 2173.05(b): "Acceptability of the claim language depends on whether one of ordinary skill in the art would understand what is claimed, *in light of the specification.*" (emphasis added by Applicants). The preamble introduces "a protein," and further references to "the protein" are not otherwise included in the claim until (amended) feature (c). Accordingly, if Applicants intended references to "protein sequence information," etc., to refer to "sequence information of the (preamble) protein," Applicants would have drafted the claim as such. As Examiner knows, the claims were *not* written to provide such association with the exception of (amended) feature (c) that clearly provides an association of "the protein" to the preamble protein. Once again, with further reference to MPEP 2173.05(b), one of ordinary skill who read the specification would understand that the claimed database includes protein data beyond protein data of the preamble's protein.

The Examiner also rejected independent claims 1 and 58 regarding the association of the correlating. As previously provided herein, Applicants amend independent claims 1 and 58 to clarify the claimed subject matter.

The Examiner indicated claim 3 lacks clarity based on the "results obtained from" language. Applicants amend claim 3 to remove the "results obtained from" language, and Applicants similarly provide new claim 65 that includes the same claimed subject matter that expresses that the biophysical property can be derived from data obtained from such methods previously claimed in dependent claim 3. No new matter is thus presented by such new claim.

The Examiner states that claim 58 recites "the experimental procedures" without providing antecedent basis. Applicants amend independent claim 58 accordingly to remove the issue regarding lack of antecedent basis.

Based on the above remarks, Applicants traverse Examiner's rejections of claims 1-3, 5, 38-43, and 58-64 under 35 U.S.C. §112, second paragraph.

Rejection of claims 1-3, 5, 38 and 39 under 35 U.S.C. 102(b)

Claims 1-3, 5, 38 and 39 were rejected under 35 U.S.C. §102(b) as being anticipated by Payne et al., Nucleic Acids Research, 25: 57-62 (1997). The Action states that:

> Payne et al demonstrates a proteomic yeast database of Saccharomyces cerevisiae that includes protein sequence information and protein property information ... as required by claim 1. The database includes analysis tools for data mining, maintained by Martins-Reid Institute for Protein Sequences .... A data mining technique such as the decision tress analysis as seen in claims 38 and 39, is demonstrated by simple decision-making analysis tools deciding what correlations exist, or not, between protein biophysical properties and sequence data. (Office Action at 7)

The rejection is respectfully traversed.

Payne et al. discloses a database that "provides a comprehensive description of the proteins of Saccharomayces cerevisiae" (Payne et al., at page 57, left column, first paragraph). Each protein is contained in the database in the form of a report and users can access the reports through search forms or indexes (Payne et al. at page 57, right column, second complete paragraph). The protein reports include sequence information and other information related to a protein based on a literature review (Payne et al., at page 57). The database is described as a curatorial effort relating to yeast protein information (Payne et al., at page 62). However, contrary to the assertions in the Office Action, Payne et al. does *not* teach a *method for determining at least one of the biochemical and biophysical properties* of a protein by *analyzing* a database using a data-mining technique to *correlate* one or more of protein sequence, biochemical properties, and/or biophysical properties. The YPD database taught by Payne et al. does not include analysis tools for data mining, maintained by Martins-Reid Institute for Protein Sequences as stated in the Office Action. Rather, Payne et al. states that their YPD database is linked to a *genome* database maintained by the Martinsreid Institute for Protein Sequences which contains analysis tools. It is not clear what types of analysis these tools are capable of nor whether they may even be used to analyze the data in the YPD database. Payne et al. merely discloses an archive of yeast protein information from which users may retrieve a record. Payne et al. clearly does not teach a method for determining at least one of the

biochemical and biophysical properties of a protein by analyzing a database using a data-mining technique to correlate one or more of protein sequence, biochemical properties, and/or biophysical properties.

A claim is anticipated only if each and every element of the claim is found in a single prior art reference. The Payne et al. reference does not teach each and every element of the claims in the present application. Therefore, reconsideration and withdrawal of the rejection of claims under 35 U.S.C. 102(b) is respectfully requested.
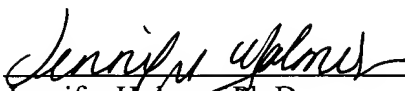
CONCLUSION

Applicants consider the Response herein to be fully responsive to the referenced Office Action. Based on the above Remarks, it is respectfully submitted that this application is in condition for allowance. Accordingly, allowance is requested. If a telephone conversation with Applicant's Attorney would expedite prosecution of the above-identified application, the Examiner is urged to call the undersigned at (617) 832-1000.

Respectfully submitted,

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